UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,786	05/14/2001	Joydeep Lahiri	SP01-129	8152

22928 7590 09/02/2004

CORNING INCORPORATED
SP-TI-3-1
CORNING, NY 14831

EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 09/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,786	LAHIRI ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 51-86* is/are pending in the application.

4a) Of the above claim(s) *4,5,12-14,20-30,57,58,65-67,71 and 73-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-11,15-19,31,32,51-56,59-64,68-70,72 and 84-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 December 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/21/03 has been entered.

Status of Claims

2. Applicant's amendment filed 8/21/03 is acknowledged and entered. Claims 1, and 51-52 have been amended. Claims 54-86 have been added.

3. It is noted that the listing of claims submitted on 6/8/2004 is improper because it did not list all the claims and their status, i.e. missing claims 4-6, 11-14, 18, 20-30, 32, 33-50, 57-59, 63-67, 73-78, 80-83, and 85, as require by 37 CFR 1.121. However since the response filed on 6/8/2004 is a bona fide response, the claims listing filed on 6/8/2004 ***will not*** replace the claims listing filed 8/21/2003.

4. Claims 33-50 were canceled by the amendment filed on 12/2/02.

5. This application claims priority to a provisional application 60/224,135 filed 8/10/2000.

6. Claims 1-32, and 51-86 are pending.

Election/Restrictions

7. Applicant has elected the following species for the elected invention (Claims 1-32, and 51-86) in the response filed on 2/24/04 and 6/8/04:

a. A species of array condition: ambient humidity.

b. A species of protein, i.e. membrane bound protein: G-protein-coupled receptor.

c. A species of substrate: glass.

d. A species of substrate coating: γ-aminopropyl silane.

8. Applicant's election of species with traverse in the reply filed on 2/24/04 is acknowledged.

The traversal is on the grounds that "*the Examiner issued a Restriction Requirement identifying the following groups of claims as being drawn to potentially distinct inventions*" and "*that the environmental conditions (i.e., "air-water interface" or "ambient humidity") properly should not be considered as separate and distinct species. These conditions characterize certain attributes of the inventive arrays that are not necessarily mutually exclusive conditions relative to one another. In other words, an array can have the biological membranes remain both adhered to the substrate surface who drawn through an air-water interface, as well as being functional when exposed to air under ambient humidity, since one characteristic does not automatically preclude the other*".

This is not found persuasive because 1) applicant has misinterpreted the election requirement dated 11/17/03. The Office Action clearly states that "*The presently amended claimed invention (Claims 1-32, and 51-86) disclosed a plurality of patentably distinct species*", i.e. an election of species ***not*** a restriction requirement. Thus applicant argument is confusing. Additionally, each species are structurally and functionally distinct from each other, e.g. a G-protein coupled receptor as claimed in claims 3 and 56 and a tyrosine kinase receptor as claimed in claims 5 and 58 are structurally and functionally distinct, and thus the claimed membrane bound protein of claims 1 and 54 has patentably distinct species. But if applicant believe that each species are not structurally and functionally distinct from each other the examiner invite applicant to state clearly on record that each of these species are not structurally and functionally distinct.

2) Applicant argument that the species of environmental conditions, i.e. air-water interface and ambient humidity, are not separate and distinct species because of the functionality of the biological membrane, i.e. its ability to remain adhered to the substrate surface, is confusing. It is unclear how applicant would regard the characteristic (functionality) of the biological membrane to define that the species of environmental conditions are structurally and functionally equivalent. However upon reconsideration of the species requirement for the environmental conditions, the species requirement for the environmental conditions has been withdrawn.

3) Therefore species requirement for the type of membrane bound protein, the type of substrate, and the type of substrate coating are still deemed proper and is therefore made **FINAL**.

9. Claims 4-5, 12-14, 20-30, 57-58, 65-67, 71, and 73-83 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/24/04 and 6/8/04.

10. Claims 1-3, 6-11, 15-19, 31-32, 51-56, 59-64, 68-70, 72, and 84-86 are treated on the merit in this Office Action.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-3, 6-11, 15-19, 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 1 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological

membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

The specification disclosure does not sufficiently teach the scope of the claimed array wherein ***any*** combination of substrate and biological membrane microspots would result in an array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. The specification description is directed to a list of ***all*** possible types of substrate (see specification paragraph [0038]), a list of ***all*** possible types of substrate coating (see specification paragraphs: [0041]-[0049]), and a list of ***all*** possible types of biological membrane (see specification paragraph [0050]). The specification single example is drawn to an array wherein the substrate is an γ-aminopropyl silane coated glass slide and the biological membrane microspots are G-protein coupled receptor. This array was tested for its stability under environmental condition of air-water interface wherein the biological membrane remained adsorbed when drawn through an air-water interface (see specification paragraph [0076] and fig. 3). This array clearly does not provide an adequate representation regarding the scope of the claimed array wherein ***any*** combination of substrate and biological membrane microspots would result in an array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. Thus the specification does not teach the claimed array of ***any*** combination of substrate and biological membrane microspots that would result in an array wherein the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of an array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor that is stable when the drawn through an air-water interface disclosed by the specification, the skilled artisan cannot envision the claimed array of ***any*** combination of substrate and biological membrane microspots that would result in an array wherein the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with

the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the claimed array of ***any*** combination of substrate and biological membrane microspots that would result in an array wherein the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. Therefore, only the array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor that is stable when the drawn through an air-water interface, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

13. Claims 52-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 52 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity. This limitation is interpreted as a functional limitation of the array wherein the ability substrate result in an array that can to be produced, used, or stored in an environment exposed to air under ambient humidity.

The specification disclosure does not sufficiently teach the scope of the claimed array wherein ***any*** substrate would result in an array that can to be produced, used, or stored in an environment exposed to air under ambient humidity. The specification description is directed to a list of ***all*** possible types of substrate (see specification paragraph [0038]), a list of ***all*** possible types of substrate coating (see specification paragraphs: [0041]-[0049]), and the preferred substrate is the commercially available γ-aminopropyl silane coated glass slide of Corning, Inc., i.e. CMT-GAPS™ glass slide, (see specification paragraph [0042]). The specification description is also directed to the known printing technique and apparatus (specification paragraphs: [0053]-[0056]). The specification single example is drawn to an array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor. The G-protein coupled receptors were printed on the Corning, Inc. glass slide, i.e. CMT-GAPS™ glass slide, and incubated in a humid chamber at room temperature for one hour (see specification paragraphs: [0071], and [0074]). The array with G-protein coupled receptors is use in ligand binding experiments (see specification paragraph [0071] and [0072]). The arrays were stored in a desiccator at 4 ^{O}C (see specification paragraph [0071]). This array clearly does not provide an adequate representation regarding the scope of the claimed array wherein ***any*** substrate would result in an array that can to be produced, used, or stored in an environment exposed to air under ambient humidity. Additionally, the specification is silent in producing, using, and storing an array in an environment exposed to air under ambient humidity. Thus the specification does not teach the claimed array wherein ***any*** substrate would result in an array that can to be produced, used, or stored in an environment exposed to air under ambient humidity.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of an array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor that is made by printing, store in a desiccator at 4 ^{O}C, and use in ligand binding experiments disclosed by the specification, the skilled artisan cannot envision the claimed array wherein ***any*** substrate would result in an array that can to be produced, used, or stored in an environment exposed to air under ambient humidity. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with

the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the claimed array wherein ***any*** substrate would result in an array that can to be produced, used, or stored in an environment exposed to air under ambient humidity. Therefore, only the array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor that is made by printing, store in a desiccator at 4 ^{O}C, and use in ligand binding experiments, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

14. Claims 54-56, 59-64, 68-70, 72, and 84-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 54 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand. This limitation is interpreted as a functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

The specification disclosure does not sufficiently teach the scope of the claimed array wherein ***any*** biological membrane microspots would result in an array wherein after the array

have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. The specification description is directed to a list of ***all*** possible types of biological membrane (see specification paragraph [0050]), and a list of ***all*** possible methods of using the array (see specification paragraph: [0057]-[0067]). The specification single example is drawn to an array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor. The array was tested for its functional stability, i.e. the G-protein coupled receptor binding ability, after the array has been store under high-humidity at various temperature, i.e. room temp to -80 ^{O}C, (see specification paragraph [0075]). This array clearly does not provide an adequate representation regarding the scope of the claimed array wherein ***any*** biological membrane microspots would result in an array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. Thus the specification does not teach the claimed array wherein ***any*** biological membrane microspots would result in an array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of an array wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor, and after the array has been store under high-humidity at various temperature the G-protein coupled receptor still has the ability to bind to the ligand disclosed by the specification, the skilled artisan cannot envision the claimed array wherein ***any*** biological membrane microspots would result in an array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the claimed array wherein ***any*** biological membrane microspots would result in an array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind

to the ligand. Therefore, only the wherein the substrate is an γ-aminopropyl silane glass slide and the biological membrane microspots are G-protein coupled receptor, and after the array has been store under high-humidity at various temperature the G-protein coupled receptor still has the ability to bind to the ligand, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 52-56, 59-64, 68-70, 72, and 84-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The phrase "can be" of claim 52 is vague and indefinite because it is unclear whether the claimed array "has" the ability to be produced, used, or stored in an environment exposed to air under ambient humidity. Thus it is unclear as what constitutes the metes and bounds of the 'functionality' of the claimed array.

b) Claim 54 is vague and indefinite because it is unclear whether the membrane microspots have ability to bind to a ligand under environmental condition of ambient humidity, i.e. the assay is performed under environmental condition of ambient humidity, or that after the array have been exposed to air under ambient humidity the membrane still has the ability to bind to the ligand. Thus claim 54 is vague and indefinite.

c) Claim 86 is vague and indefinite because it is unclear whether the membrane microspots have ability to bind to a ligand under environmental condition of ambient humidity, i.e. the assay is performed under environmental condition of ambient humidity, or that after the array have been exposed to air under ambient humidity the membrane still has the ability to bind to the ligand. Thus claim 86 is vague and indefinite.

17. Claims 1-3, 6-11, 15-19, 31-32, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: The structural limitation of the substrate that makes it able to be "*adapted so that the microspots remain adsorbed when the drawn through an air-water interface*", i.e. it is the type of linker or glue that makes the microspots remain adhered to the substrate.

18. Claims 52-53 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: The structural limitation of the substrate that makes it able to be "*adapted so that the array can be produced, used, or stored in an environment exposed to air under ambient humidity*".

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1, 6-9, 15, and 31-32 are rejected under 35 U.S.C. 102(b) as anticipated by The President and Fellows of Harvard College (which is now refer to as Harvard) (WO 98/16830).

The instant claim 1 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

Harvard discloses an assay system and its uses for identifying compounds having desirable biological activities (see e.g. Abstract; pg. 2, lines 2-10). The assay system comprises a displayed surface (refers to a substrate) and individual liquid droplets (refers to microspots) (refers to claim 1) (see e.g. pg. 5, lines 8-9 and 20-22; pg. 9, lines 24-31; pg. 10, lines 19-29; fig. 2). The displayed surface includes material such as plastic, or glass (refers to claim 6) (see e.g. pg. 9, lines 30-31). The droplets include material such as cell (refers to biological membrane) (see e.g. pg. 10, lines 24-26; fig. 2). On example of an assay system disclose a fibronectin-coated glass coverslip and the droplets are fibroblasts (refers to claims 1, 6-9, 15, and 31-32) (see e.g. pg. 11, lines 6-9). Harvard also discloses an assay system wherein the displayed surface is movable from one growth medium to another (refers to the functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under

environmental condition of air-water interface) (see e.g. pg. 10, lines 21-28; fig. 2). Thus, the assay system of Harvard anticipates the presently claimed array.

21. Claims 1-3, 6-9, 11, and 32 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hui et al. (US Patent 5,919,576).

The instant claim 1 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

Hui et al. teach a composition of supported biological membranes and methods of making the supported biological membranes (see e.g. Abstract; col. 1, lines 9-15; col. 2, lines 44-59). The composition (refers to the array) comprises a support such as glass, or metal (refers to claims 1, 6-7, and 32) (see e.g. col. 4, lines 34-39; col. 5, lines 26-36) and biological membranes (refers to claims 1-2) (see e.g. col. 3, line 64 to col. 4, line 15). The surface of the support further comprises an alkanethiol self-assembled monolayer (refers to claims 8-9, 11, and 22) (see e.g. col. 4, lines 40-50). Thus, the composition of Hui et al. teaches all the structural limitation of the presently claimed array.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface*", i.e. the functional limitation of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a

showing of unobvious differences. The structural features of the array of Hui et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

22. Claims 1-3, 6-9, 11, and 32 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108).

The instant claim 1 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col.,

line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip (refers to claims 1, 6-7, and 32), and G protein-coupled receptors (refers to claims 1-3) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (refers to claims 8-9, 11, and 22) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). Thus, the array of Bieri et al. teaches all the structural limitation of the presently claimed array.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface*", i.e. the functional limitation of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Bieri et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

23. Claims 52-53 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hui et al. (US Patent 5,919,576).

The instant claim 52 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity. Claim 52 is interpreted as a product-by-process limitation wherein the processes are method of making, and using of the array.

Hui et al. teach a composition of supported biological membranes and methods of making the supported biological membranes (see e.g. Abstract; col. 1, lines 9-15; col. 2, lines 44-59). The composition (refers to the array) comprises a support such as glass, or metal (see e.g. col. 4, lines 34-39; col. 5, lines 26-36) and biological membranes (refers to claim 52) (see e.g. col. 3, line 64 to col. 4, line 15). The surface of the support further comprises an alkanethiol self-assembled monolayer (refers to claim 53) (see e.g. col. 4, lines 40-50). Thus, the composition of Hui et al. teaches all the structural limitation of the presently claimed array.

The limitation "*the surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity*" of instant claim 52 is interpreted to be process limitations and thus the instant claim 52 is written as product-by-process claims. "Eventhough the product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. The patentability is based on the **product itself** that is the array of the instant claims. Bieri et al. teach the presently claimed array. If the product in the product-by-process claims is same or as obvious from the

product of the prior art, the claim is unpatentable eventhough the prior art product was made by a different process." *In re* Thorpe, 777 F. 2d 695, 698, 227 U. S. P. Q. 964, 966 (Fed. Cir. 1985). (See MPEP 2113).

Thus, alternatively the claimed invention further differs from the prior art teachings only by the recitation of "*the surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity*", i.e. the process limitations of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the array can be produced, used, or stored in an environment exposed to air under ambient humidity. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989).

24. Claims 52-53 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108).

The instant claim 52 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity. Claim

52 is interpreted as a product-by-process limitation wherein the processes are method of making, and using of the array.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col., line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip, and G protein-coupled receptors (refers to claim 52) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (refers to claim 53) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). Thus, the array of Bieri et al. teaches all the structural limitation of the presently claimed array.

The limitation "*the surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity*" of instant claim 52 is interpreted to be process limitations and thus the instant claim 52 is written as product-by-process claims. "Eventhough the product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. The patentability is based on the **product itself** that is the array of the instant claims. Bieri et al. teach the presently claimed array. If the product in the product-by-process claims is same or as obvious from the product of the prior art, the claim is unpatentable eventhough the prior art product was made by a different process." In re Thorpe, 777 F. 2d 695, 698, 227 U. S. P. Q. 964, 966 (Fed. Cir. 1985). (See MPEP 2113).

Thus, alternatively the claimed invention further differs from the prior art teachings only by the recitation of "*the surface of the substrate is adapted such that the array can be produced, used, or stored in an environment exposed to air under ambient humidity*", i.e. the process limitations of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the array can be produced, used, or stored in an environment exposed to air under ambient humidity. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989).

25. Claims 54-56, 59-61, 64, and 85 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hui et al. (US Patent 5,919,576).

The instant claim 54 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand. This limitation is interpreted as a functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

Hui et al. teach a composition of supported biological membranes and methods of making the supported biological membranes (see e.g. Abstract; col. 1, lines 9-15; col. 2, lines 44-59).

The composition (refers to the array) comprises a support such as glass, or metal (refers to claims 54, 59-60, and 85) (see e.g. col. 4, lines 34-39; col. 5, lines 26-36) and biological membranes (refers to claims 54-55) (see e.g. col. 3, line 64 to col. 4, line 15). The surface of the support further comprises an alkanethiol self-assembled monolayer (refers to claims 61-62, 64, and 75) (see e.g. col. 4, lines 40-50). Thus, the composition of Hui et al. teaches all the structural limitation of the presently claimed array.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand*", i.e. the functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Hui et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

26. Claims 54-56, 59-62, 64, and 85 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108).

The instant claim 54 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand. This limitation is interpreted as a functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col., line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip (refers to claims 54, 59-60, and 85), and G protein-coupled receptors (refers to claims 54-56) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (refers to claims 61-62, 64, and 75) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). Thus, the array of Bieri et al. teaches all the structural limitation of the presently claimed array.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand*", i.e. the functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on

the substrate still has the ability to bind to the ligand. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Bieri et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claims 1-3, 6-11, 15-19, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108) and Patton (US Patent 4,933,285).

The instant claim 1 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col., line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip (refers to claims 1, 6-7, and 32), and G protein-coupled receptors (refers to claims 1-3) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (refers to claims 8-9, 11, and 22) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). Thus Bieri et al. teaches all the structural limitation of the presently claimed array of claim 1.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the substrate is adapted such that the microspots remain adsorbed when the*

drawn through an air-water interface", i.e. the functional limitation of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Bieri et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Furthermore with regard to claim 10, the instant claim limitation of the contact angle of the substrate coating is either inherently present in the coating material or constitute obvious variations in parameters which are routinely modified in the art (e.g. the thickness of the coating on the substrate), and which have not been described as critical to the practice of the invention.

The array of Bieri et al. does not expressly include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane).

Patton teaches a structure for immobilization of macromolecules or other biomolecules and the process of making such a structure (see e.g. Abstract; col. 1, lines 10-17; col. 2, lines 54-65). The structure comprising monolayers of polymeric linkages used as biochemical sensors

(see e.g. col. 1, lines 10-17). The substrate includes inorganics such as silicon or silicon oxide (refers to glass), natural and synthetic polymers, and metals such as gold (see e.g. col. 3, lines 35-68 to col. 4, lines 1-6). The polymeric linkage is bifunctional with functional groups such as amino groups, or alcohols (see e.g. col. 2, lines 22-38). The silicon oxide layer is covalently linked to gamma-aminopropylsilane (see e.g. col. 4, lines 7-25). The polymeric linkage would provide enhanced stabilities of the immobilized biomolecules (see e.g. col. 15, lines 8-20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) as taught by of Patton in the array of Bieri et al. One of ordinary skill in the art would have been motivated to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) in the array of Bieri et al. for the advantage of providing for a polymeric linkage would provide enhanced stabilities of the immobilized biomolecules and the choice of substrate such as plastic or glass would provide the advantage of economy and convenience. (Patton: col. 15, lines 8-20). Since both Bieri et al. and Patton disclose a process of immobilized structure comprising multiple monolayers of effective sequential polymeric linkages is built from the surface of a solid phase (Bieri: pg. 1108, left col., lines 23-40; Patton: col. 2, lines 54-59). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Bieri et al. and Patton because Patton disclose the by example the immobilization of a protein on a glass substrate (Patton: col. 19, lines 16-24).

30. Claims 1-3, 6-11, 15-19, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hui et al. (US Patent 5,919,576) and Patton (US Patent 4,933,285).

The instant claim 1 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

Hui et al. teach a composition of supported biological membranes and methods of making the supported biological membranes (see e.g. Abstract; col. 1, lines 9-15; col. 2, lines 44-59). The composition (refers to the array) comprises a support such as glass, or metal (refers to claims 1, 6-7, and 32) (see e.g. col. 4, lines 34-39; col. 5, lines 26-36) and biological membranes (refers to claims 1-2) (see e.g. col. 3, line 64 to col. 4, line 15). The surface of the support further comprises an alkanethiol self-assembled monolayer (refers to claims 8-9, 11, and 22) (see e.g. col. 4, lines 40-50). Thus, the composition of Hui et al. teaches all the structural limitation of the presently claimed array of claim 1.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface*", i.e. the functional limitation of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Hui et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the

factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Furthermore with regard to claim 10, the instant claim limitation of the contact angle of the substrate coating is either inherently present in the coating material or constitute obvious variations in parameters which are routinely modified in the art (e.g. the thickness of the coating on the substrate), and which have not been described as critical to the practice of the invention.

The array of Hui et al. does not expressly disclose that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane)..

Patton teaches a structure for immobilization of macromolecules or other biomolecules and the process of making such a structure (see e.g. Abstract; col. 1, lines 10-17; col. 2, lines 54-65). The structure comprising monolayers of polymeric linkages used as biochemical sensors (see e.g. col. 1, lines 10-17). The substrate includes inorganics such as silicon or silicon oxide (refers to glass), natural and synthetic polymers, and metals such as gold (see e.g. col. 3, lines 35-68 to col. 4, lines 1-6). The polymeric linkage is bifunctional with functional groups such as amino groups, or alcohols (see e.g. col. 2, lines 22-38). The silicon oxide layer is covalently

linked to gamma-aminopropylsilane (see e.g. col. 4, lines 7-25). The polymeric linkage would provide enhanced stabilities of the immobilized biomolecules (see e.g. col. 15, lines 8-20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) as taught by of Patton in the array of Bieri et al. One of ordinary skill in the art would have been motivated to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) in the array of Bieri et al. for the advantage of providing for a polymeric linkage would provide enhanced stabilities of the immobilized biomolecules and the choice of substrate such as plastic or glass would provide the advantage of economy and convenience. (Patton: col. 15, lines 8-20). Since both Bieri et al. and Patton disclose a process of immobilized structure comprising multiple monolayers of effective sequential polymeric linkages is built from the surface of a solid phase (Bieri: pg. 1108, left col., lines 23-40; Patton: col. 2, lines 54-59). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Bieri et al. and Patton because Patton disclose the by example the immobilization of a protein on a glass substrate (Patton: col. 19, lines 16-24).

31. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108) and Patton (US Patent 4,933,285).

The instant claim 51 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is a glass substrate wherein the surface is coated with γ-aminopropyl silane. The biological membrane microspot is G-protein-coupled

receptor. The substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface. This limitation is interpreted as a functional limitation of the array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col., line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip, and G protein-coupled receptors (refers to claim 51) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40).

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the substrate is adapted such that the microspots remain adsorbed when the drawn through an air-water interface*", i.e. the functional limitation of the array. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein the ability of the substrate to "hold onto" the biological membrane microspots and/or the ability of the biological membrane microspots to remain "attached" to the substrate under environmental condition of air-water interface. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See

In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

The array of Bieri et al. does not expressly include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane).

Patton teaches a structure for immobilization of macromolecules or other biomolecules and the process of making such a structure (see e.g. Abstract; col. 1, lines 10-17; col. 2, lines 54-65). The structure comprising monolayers of polymeric linkages used as biochemical sensors (see e.g. col. 1, lines 10-17). The substrate includes inorganics such as silicon or silicon oxide (refers to glass), natural and synthetic polymers, and metals such as gold (see e.g. col. 3, lines 35-68 to col. 4, lines 1-6). The polymeric linkage is bifunctional with functional groups such as amino groups, or alcohols (see e.g. col. 2, lines 22-38). The silicon oxide layer is covalently linked to gamma-aminopropylsilane (see e.g. col. 4, lines 7-25). The polymeric linkage would provide enhanced stabilities of the immobilized biomolecules (see e.g. col. 15, lines 8-20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) as taught by of Patton in the array of Bieri et al. One of ordinary skill in the art would have been motivated to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) in the array of Bieri et al. for the advantage of providing for a polymeric linkage would provide enhanced stabilities of the immobilized biomolecules and the choice of substrate such as plastic or glass would provide the advantage of economy and convenience. (Patton: col. 15, lines 8-20). Since both Bieri et al. and Patton

disclose a process of immobilized structure comprising multiple monolayers of effective sequential polymeric linkages is built from the surface of a solid phase (Bieri: pg. 1108, left col., lines 23-40; Patton: col. 2, lines 54-59). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Bieri et al. and Patton because Patton disclose the by example the immobilization of a protein on a glass substrate (Patton: col. 19, lines 16-24).

32. Claims 54-56, 59-64, 68-70, 72, and 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108) and Patton (US Patent 4,933,285).

The instant claim 54 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand. This limitation is interpreted as a functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col., line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip (refers to claims 54, 59-60, and 85), and G protein-coupled receptors (refers to claims 54-56) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (refers to claims 61-62, 64, and 75) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-

29; pg. 1108, lines 24-40). Thus, the array of Bieri et al. teaches all the structural limitation of the presently claimed array of claim 54.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand*", i.e. the functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Bieri et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Furthermore with regard to claim 63, the instant claim limitation of the contact angle of the substrate coating is either inherently present in the coating material or constitute obvious variations in parameters which are routinely modified in the art (e.g. the thickness of the coating on the substrate), and which have not been described as critical to the practice of the invention.

The array of Bieri et al. does not expressly include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane).

Patton teaches a structure for immobilization of macromolecules or other biomolecules and the process of making such a structure (see e.g. Abstract; col. 1, lines 10-17; col. 2, lines 54-65). The structure comprising monolayers of polymeric linkages used as biochemical sensors (see e.g. col. 1, lines 10-17). The substrate includes inorganics such as silicon or silicon oxide (refers to glass), natural and synthetic polymers, and metals such as gold (see e.g. col. 3, lines 35-68 to col. 4, lines 1-6). The polymeric linkage is bifunctional with functional groups such as amino groups, or alcohols (see e.g. col. 2, lines 22-38). The silicon oxide layer is covalently linked to gamma-aminopropylsilane (see e.g. col. 4, lines 7-25). The polymeric linkage would provide enhanced stabilities of the immobilized biomolecules (see e.g. col. 15, lines 8-20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) as taught by of Patton in the array of Bieri et al. One of ordinary skill in the art would have been motivated to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) in the array of Bieri et al. for the advantage of providing for a polymeric linkage would provide enhanced stabilities of the immobilized biomolecules and the choice of substrate such as plastic or glass would provide the advantage of economy and convenience. (Patton: col. 15, lines 8-20). Since both Bieri et al. and Patton disclose a process of immobilized structure comprising multiple monolayers of effective sequential polymeric linkages is built from the surface of a solid phase (Bieri: pg. 1108, left col.,

lines 23-40; Patton: col. 2, lines 54-59). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Bieri et al. and Patton because Patton disclose the by example the immobilization of a protein on a glass substrate (Patton: col. 19, lines 16-24).

33. Claims 54-55, 59-64, 68-70, 72, and 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hui et al. (US Patent 5,919,576) and Patton (US Patent 4,933,285).

The instant claim 54 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand. This limitation is interpreted as a functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

Hui et al. teach a composition of supported biological membranes and methods of making the supported biological membranes (see e.g. Abstract; col. 1, lines 9-15; col. 2, lines 44-59). The composition (refers to the array) comprises a support such as glass, or metal (refers to claims 54, 59-60, and 85) (see e.g. col. 4, lines 34-39; col. 5, lines 26-36) and biological membranes (refers to claims 54-55) (see e.g. col. 3, line 64 to col. 4, line 15). The surface of the support further comprises an alkanethiol self-assembled monolayer (refers to claims 61-62, 64, and 75) (see e.g. col. 4, lines 40-50). Thus, the composition of Hui et al. teaches all the structural limitation of the presently claimed array of claim 54.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the plurality of biological membrane microspots when exposed to air under*

ambient humidity still has the ability to bind to a ligand", i.e. the functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the array of Hui et al. are the same as the structural features of the claimed array, which are a substrate and a plurality of biological membrane microspots. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Furthermore with regard to claim 63, the instant claim limitation of the contact angle of the substrate coating is either inherently present in the coating material or constitute obvious variations in parameters which are routinely modified in the art (e.g. the thickness of the coating on the substrate), and which have not been described as critical to the practice of the invention.

The array of Hui et al. does not expressly disclose that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane)..

Patton teaches a structure for immobilization of macromolecules or other biomolecules and the process of making such a structure (see e.g. Abstract; col. 1, lines 10-17; col. 2, lines 54-

65). The structure comprising monolayers of polymeric linkages used as biochemical sensors (see e.g. col. 1, lines 10-17). The substrate includes inorganics such as silicon or silicon oxide (refers to glass), natural and synthetic polymers, and metals such as gold (see e.g. col. 3, lines 35-68 to col. 4, lines 1-6). The polymeric linkage is bifunctional with functional groups such as amino groups, or alcohols (see e.g. col. 2, lines 22-38). The silicon oxide layer is covalently linked to gamma-aminopropylsilane (see e.g. col. 4, lines 7-25). The polymeric linkage would provide enhanced stabilities of the immobilized biomolecules (see e.g. col. 15, lines 8-20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) as taught by of Patton in the array of Bieri et al. One of ordinary skill in the art would have been motivated to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) in the array of Bieri et al. for the advantage of providing for a polymeric linkage would provide enhanced stabilities of the immobilized biomolecules and the choice of substrate such as plastic or glass would provide the advantage of economy and convenience. (Patton: col. 15, lines 8-20). Since both Bieri et al. and Patton disclose a process of immobilized structure comprising multiple monolayers of effective sequential polymeric linkages is built from the surface of a solid phase (Bieri: pg. 1108, left col., lines 23-40; Patton: col. 2, lines 54-59). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Bieri et al. and Patton because Patton disclose the by example the immobilization of a protein on a glass substrate (Patton: col. 19, lines 16-24).

34. Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieri et al. (*Nature Biotechnology*, **11/1999**, 17(11):1105-1108) and Patton (US Patent 4,933,285).

The instant claim 51 recites an array. The array comprises a substrate and a plurality of biological membrane microspots. The substrate is a glass substrate wherein the surface is coated with γ-aminopropyl silane. The biological membrane microspot is G-protein-coupled receptor. The plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand. This limitation is interpreted as a functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand.

Bieri et al. teach an array of micropatterned immobilization of a G-protein-coupled receptor and the method of detecting G protein activation (see e.g. Abstract; pg. 1105, right col., line 15 to pg. 1106, left col. Line 3; pg. 1106, lines 16-29; fig. 1). The array comprises a gold surface sensor chip (refers to claims 54, 59-60, and 85), and G protein-coupled receptors (refers to claims 54-56) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40). The surface is treated with ω-hydroxy-undecanethiol and biotinylated-thiol moieties (refers to claims 61-62, 64, and 75) (see e.g. pg. 1105, right col., lines 15-29; pg. 1106, lines 16-29; pg. 1108, lines 24-40).

Alternatively, the claimed invention further differs from the prior art teachings only by the recitation of "*the plurality of biological membrane microspots when exposed to air under ambient humidity still has the ability to bind to a ligand*", i.e. the functional limitation of the array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious

differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference array wherein after the array have been exposed to air under ambient humidity the membrane on the substrate still has the ability to bind to the ligand. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

The array of Bieri et al. does not expressly include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane).

Patton teaches a structure for immobilization of macromolecules or other biomolecules and the process of making such a structure (see e.g. Abstract; col. 1, lines 10-17; col. 2, lines 54-65). The structure comprising monolayers of polymeric linkages used as biochemical sensors (see e.g. col. 1, lines 10-17). The substrate includes inorganics such as silicon or silicon oxide (refers to glass), natural and synthetic polymers, and metals such as gold (see e.g. col. 3, lines 35-68 to col. 4, lines 1-6). The polymeric linkage is bifunctional with functional groups such as amino groups, or alcohols (see e.g. col. 2, lines 22-38). The silicon oxide layer is covalently linked to gamma-aminopropylsilane (see e.g. col. 4, lines 7-25). The polymeric linkage would provide enhanced stabilities of the immobilized biomolecules (see e.g. col. 15, lines 8-20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) as taught by of Patton in the

array of Bieri et al. One of ordinary skill in the art would have been motivated to include that the type of substrate is plastic or glass substrate and coating material such as gamma-aminopropylsilane (γ-aminopropyl silane) in the array of Bieri et al. for the advantage of providing for a polymeric linkage would provide enhanced stabilities of the immobilized biomolecules and the choice of substrate such as plastic or glass would provide the advantage of economy and convenience. (Patton: col. 15, lines 8-20). Since both Bieri et al. and Patton disclose a process of immobilized structure comprising multiple monolayers of effective sequential polymeric linkages is built from the surface of a solid phase (Bieri: pg. 1108, left col., lines 23-40; Patton: col. 2, lines 54-59). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Bieri et al. and Patton because Patton disclose the by example the immobilization of a protein on a glass substrate (Patton: col. 19, lines 16-24).

Withdrawn Objections and /or Rejections

35. The rejection of claim 53 under 35 USC 112, first paragraph (new matter rejection) has been withdrawn in light of applicant's arguments, see pages 15-16, filed 8/21/03.

Response to Arguments

36. Applicant's arguments with respect to claims 1-32, and 51-53 have been considered but are moot in view of the new grounds of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
August 30, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER